≥ *Original Article* ≤

Feasibility of Endovascular Abdominal Aortic Aneurysm Repair Outside of the Instructions for Use and Morphological Changes at 3 Years after the Procedure

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Introduction: We retrospectively analyzed outcomes of patients who had undergone endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) more than 3 years previously in a single institution. We compared outcomes between patients who underwent EVAR within and outside of the devices' instructions for use (IFU) and examined mid-term morphological changes in AAA.
Methods: A total of 275 patients who underwent EVAR for AAA were selected. IFU parameters included aneurysmal neck length, angulation and presence of massive atheroma. Patients were divided into 2 groups: the Within IFU group (W-IFU: n = 193) and the Outside of IFU group (O-IFU: n = 82).
Results: Patients in the O-IFU group were older and had a larger AAA diameter. Other comorbid factors were similar between the 2 groups. There was no difference in overall survival rates and reintervention rates between the 2 groups. The most common cause for reintervention was AAA enlargement 3 years after EVAR. Irrespective of the IFU, mid-term morphological changes, including neck angulation, neck diameter, sac re-expansion, and Palmaz stent displacement, were found.
Conclusion: Outcomes of EVAR were considered acceptable in the O-IFU group. Careful follow-up is necessary considering the morphological changes in AAAs after EVAR.

Keywords: instructions for use, endovascular aneurysm repair, abdominal aortic aneurysm, morphological change

Introduction

In 2006, endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) was introduced and approved in Japan under unique circumstances.[1)]

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The Japanese Committee for Stentgraft management (JACSM) was established to ensure the safety of EVAR procedures by developing a system in which trained surgeons could supervise the inexperienced ones. Thus, the learning curve was successfully lowered and excellent midterm outcomes were reported, even in patients with a hostile anatomy.[2)]

Although anatomical factors should be a limitation for EVAR and device companies have established instructions for use (IFU), endovascular surgeons sometimes have no choice but to disregard the IFU in AAA patients with high comorbid risks. In some studies on the results of EVAR outside of IFU, aneurysmal neck factors (short length, severe angulation, and presence of massive atheroma) are commonly reported to cause EVAR-related adverse events.[3–6)]

We set these neck factors as the IFU parameters and retrospectively analyzed mid- to long-term outcomes for patients who underwent EVAR within and outside of the IFU. In addition, we examined mid-term morphological changes in AAAs.

Patients and Methods

A series 275 patients who underwent EVAR for AAA in Morinomiya Hospital (Osaka, Japan) between December 2006 and September 2009 were selected. Devices used in the series were Cook Zenith™ (Zenith: Cook Incorporated, Bloomington, Indiana, USA) and Gore Excluder™ (Excluder: W.L. Gore & Associates, Incorporated, Flagstaff, Arizona, USA): these were both same-version devices.[7,8]

Among the IFU parameters, three aneurysmal neck factors were selected: short length, severe angulation, and massive atheromatous neck. The definitions of neck factors were as follows: (1) length of aneurysmal neck <15 mm, (2) angulation of infrarenal neck ≥60 degrees (measured using the method described previously),[9] and (3) massive neck atheroma with a thickness and length ≥5 mm and circumference ≥75%.[6] Patients who had at least one of three factors were classified as Outside of the IFU (O-IFU) group, and the others were classified as Within the IFU (W-IFU) group. There were 82 patients in the O-IFU group: 25 had short length; 50, severe angulation; and 16, massive atheroma necks (in 9 patients, two factors overlapped).

While treating patients in the O-IFU group, we performed EVAR carefully using several methods. First, we used a previously reported algorithm for intraoperative management of proximal neck fixation.[2] When we identified a type 1a endoleak during intraoperative angiography, we performed a "touch-up" procedure using a semi-compliant occlusion balloon. If the endoleak did not stop, we changed the balloon to a non-compliant one and then used an aortic cuff or a Palmaz stent as the last resort. Second, device selection was based on the following principle: Zenith, which possesses a suprarenal stent hook, was preferred in cases with a short neck, and the flexible Excluder was preferred in AAAs with a torturous anatomy. Third, touch-up with a compliant balloon or attachment of Palmaz stent was contraindicated in patients with massive neck atheroma, even in the presence of a type 1a endoleak.

Reintervention was performed for (1) sac enlargement more than 10 mm, (2) graft limb migration more than 10 mm, (3) limb occlusion, (4) graft infection which was not controlled with antibiotics, and (5) others; such as bailing out the renal artery covered by the stent graft or re-touching up on the stent graft for type 1 and 3 endoleaks.

Patient outcomes after EVAR were analyzed by considering the following factors: changes in aneurysmal diameter, neck angulation, and neck diameter; types of remaining endoleaks; and displacement of the Palmaz™ XL (Cordis, Johnson & Johnson, Tokyo, Japan) stent on the proximal attachment site.

Follow up imaging examination was performed by contrast-enhanced CT every 6 months. We substituted plain CT and ultrasonography in cases with allergy of contrast medium and renal dysfunction. Follow up periods were 38.5 ± 16.7 (months) in the W-IFU group, and 32.7 ± 17.9 (months) in the O-IFU group. During the follow up periods, 36 patients died in the W-IFU group, and 21 died in the O-IFU group, respectively.

The intra-group differences were analyzed using an unpaired Student's *t*-test. We used the log-rank test to detect differences between the 2 groups. Values are reported as mean ± standard deviation. The level of significance was set at p <0.05.

Results

Baseline patient characteristics, including age, gender, and maximal anteroposterior aneurysm diameter, are shown in **Table 1**. In the O-IFU group, the patients were older (p = 0.035) and the maximal aneurysm diameter was greater (p = 0.003). The comorbid risks, including advanced age (≥80 years), respiratory failure, cerebrovascular disease, ischemic heart disease, hypertension, diabetes mellitus, chronic kidney disease, and hostile abdomen, are also shown in **Table 1**. There was no significant difference in the presence of comorbid risks between the 2 groups.

The difference in overall survival rates between the 2 groups was not statistically significant (p = 0.079) (**Fig. 1**). The difference in reintervention-free rates was not statistically significant between the 2 groups (p = 0.063) (**Fig. 2**). The causes of reintervention included dilatation of the AAA sac, migration,

Table 1 Baseline patient characteristics of the Within IFU and the Outside of IFU cohorts

Variables	Within IFU	Outside of IFU	p value
	n=193	n=82	
Age	74.8 ± 8.2	77.1 ± 7.9	0.03
Female sex, n (%)	33 (17.1%)	22 (26.8%)	0.05
Aneurymal diameter (antero-posterior) (mm)	51.8 ± 9.4	55.4 ± 10.0	0.003
Devices			
Cook Zenith	78	40	
Gore Excluder	115	42	
Comorbidities			
Elder age (>80)	61	34	0.10
Respiratory failure	47	26	0.43
Cerebrovascular disease	24	14	0.45
Ischemic heart disease	29	22	0.70
Hypertension	101	69	0.52
Diabetes mellitus	21	10	0.36
Chronic kidney disease	35	25	0.22
Hostile abdomen	41	39	0.24

IFU: instructions for use
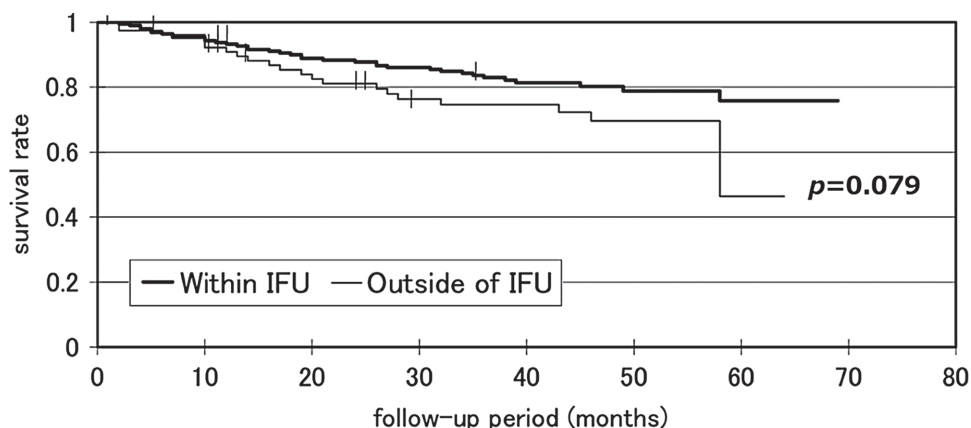
Fig. 1 Overall survival rate. There was no statistically significant difference between groups. IFU: instructions for use.

limb occlusion, infection, and others. There were 3 cases of ruptured aneurysm subsequent to sac dilatation: 2 in the W-IFU group and 1 in the O-IFU group. Several of the events that caused reintervention occurred within a short period, especially in the O-IFU group. Three years after the initial operation in both groups, most of the reinterventions were performed because of AAA sac dilatation (**Fig. 3**).

Mid-term outcomes after EVAR are described in **Table 2**. The ratio of patients who demonstrated reduction and expansion of the AAA sac was not significantly different between the 2 groups (p = 0.52).

Interestingly, among the patients with >5-mm reduction in the aneurysm diameter, approximately 10% of the patients (11 patients in 100, in the W-IFU group; 3 in 37, in the O-IFU group; respectively) in both groups showed re-expansion by >5 mm. There were no significant differences in the number of endoleaks between the 2 groups, but interestingly, type 1 and 3 endoleaks were found only in the W-IFU group, not in the O-IFU group. Chronological changes of >10 degrees in neck angulation were found more frequently in the O-IFU group (p <0.001). In the mid-term follow-up, more than 20% of patients
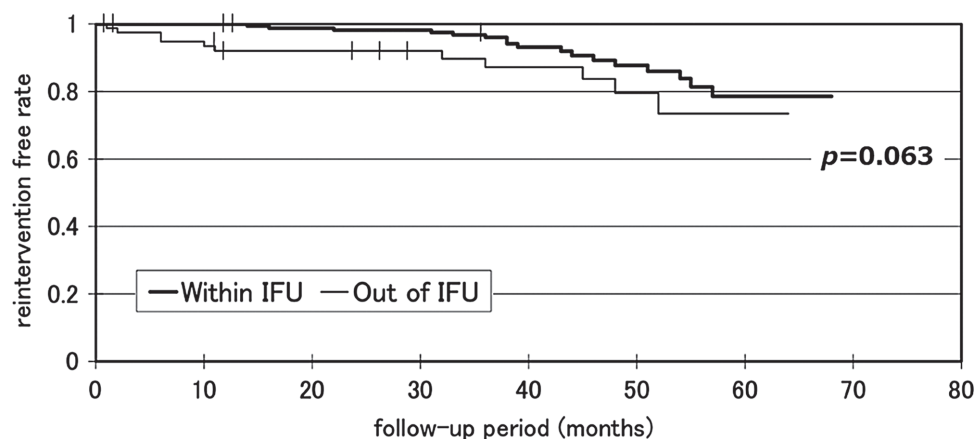
Fig. 2   Reintervention-free rate. There was no statistically significant difference between groups. IFU: instructions for use.

Table 2   Mid-term outcomes after stent graft implantation

Variables	Within IFU	Outside of IFU	p value
Aneurysm Diameter, n (%)			
Reduction*	100 (56%)	37 (52%)	
Re-expansion	*11/100*	*3/37*	
No change	60 (34%)	29 (51%)	0.52
Expansion	17 (10%)	5 (7%)	
Endoleaks			
Type 1	2	0	0.70
Type 2	42	10	
Type 3–5	1	0	
Neck angulation change, n (%)	1 (1%)	10 (18%)	<0.001
Neck diameter dilatation, n (%)	44 (23%)	23 (30%)	0.24
Palmaz stent displacement, n (%)	13 (72%)	10 (100%)	0.06

The asterisk indicates that re-expansion was assessed in patients showing reduction in aneurysm diameter. IFU: instructions for use

in both groups showed aneurysm neck dilatation, and the most of the patients who had initially added Palmaz stent showed the stent displacement (floating) (**Table 2**). However, there was no difference in dilatation of the neck diameter by >3 mm and Palmaz stent displacement between the 2 groups.

Discussion

Selection of patients with proper AAA anatomy is essential to minimize post-EVAR complications and several factors are mentioned in the devices' IFU. In a multicenter observational study, Schanzer, et al. emphasized the low compliance with IFU guidelines, which may relate to the high postoperative sac enlargement rate.[10] Abbruzzese, et al. reported the following IFU parameters: neck diameter, length, angulation, iliac fixation length, oversizing, and iliac diameter. These researchers showed a negative effect on long-term results in patients who underwent EVAR outside of the IFU.[5] Some large studies that examined EVAR outcomes showed that the most common factors causing a poor outcome were short neck and severe neck angulation.[3–5] Massive neck atheroma was also shown to affect EVAR outcome when compared to the outcome of open surgery.[6] In our study, device oversizing did not occur. There was less difficulty in creating an access route by extending the iliac limbs along with hypogastric artery embolization or in creating an access route via a retroperitoneal approach for cases of hostile iliac anatomy. Therefore, we focused on three neck-related factors.

We initially predicted a poorer outcome in the O-IFU group; however, we were not able to show
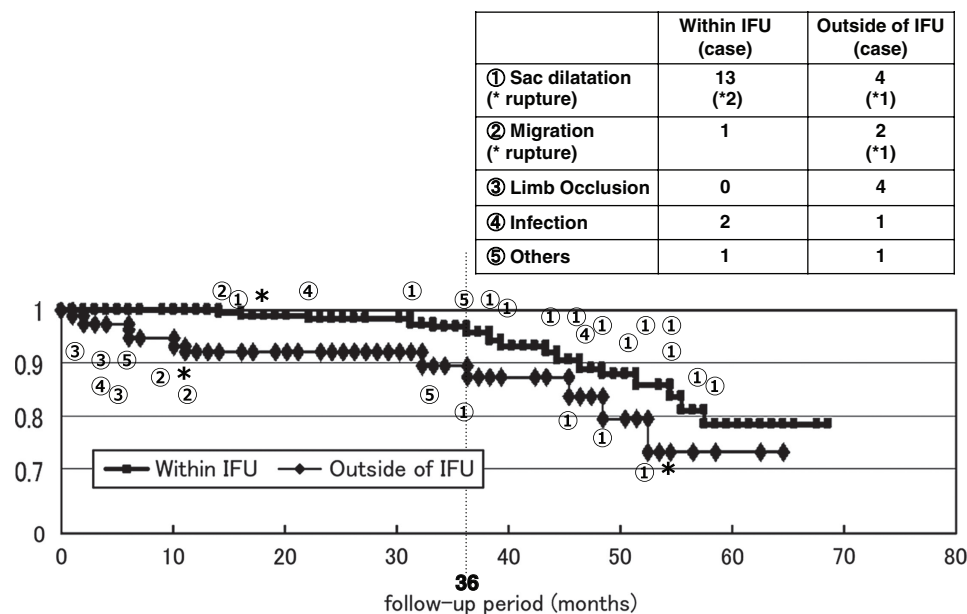
	Within IFU (case)	Outside of IFU (case)
① Sac dilatation (* rupture)	13 (*2)	4 (*1)
② Migration (* rupture)	1	2 (*1)
③ Limb Occlusion	0	4
④ Infection	2	1
⑤ Others	1	1

Fig. 3   Time points of reintervention. After 3 years, the main cause of reintervention was sac dilatation. IFU: instructions for use.

better survival rates and lesser reintervention rates in the W-IFU group. Considering the older population and larger aneurysm diameter in the O-IFU group, we concluded that the outcomes in the O-IFU group could be considered acceptable.

We were not able to find a significant difference in reintervention rate between the 2 groups, possibly due to the increase in the number of treatments needed for AAA sac dilatation, especially in the W-IFU group. We usually treated expanded aneurysms when the diameter increased by more than 5 mm compared to the initial diameter. Irrespective of IFU compliance, sac expansion occurred in approximately 10% of the cases. Considering that approximately 10% of re-expansion cases were found in the reduction group, it is necessary to pay close attention to the diameter and morphology of the aneurysm sac, even in the long term.

The cause of re-expansion remained unknown. Although more than 20% of the patients showed neck dilatation, they did not necessarily develop aneurysm re-expansion. Additionally, none of the patients in the O-IFU group showed type 1 or 3 endoleaks. Because an oversized device was usually selected initially,[11] the aneurysm neck may have been dilated to some extent in the process of graft unfolding. Paradoxical findings of less type 1 and 3 endoleaks in the

O-IFU group indicated that our careful management of patients with hostile anatomy was acceptable.[2]

In some cases, we used a Palmaz stent for preventing type 1a endoleaks, with excellent mid-term results.[2] However, Byrne, et al. recently reported that the higher rate of post-operative endoleaks, especially type 1 endoleaks, in patients who underwent EVAR with Palmaz stenting than in those without Palmaz stenting.[12] Although there was no type 1 endoleak in our study fortunately, most of the implanted Palmaz stents showed displacement and poor attachment to the proximal site. Considering the gradual neck dilatation caused by graft unfolding, an aortic cuff should be used for intraoperative type 1a endoleak instead of the Palmaz.

This study has some limitations. Although we only used 2 devices, certain long-term device-specific behaviors may affect the morphological changes in AAA. The relatively small number of patients included in this study is not sufficient for a subgroup analysis of each device. A longer follow-up period is required to evaluate the differences in reintervention rates, which might be greatly affected by the treatment of type 2 endoleak in cases of sac enlargement. We expect that the difference in survival and reintervention rates between the 2 groups will be smaller in the mid-term period.

In conclusion, outcomes of EVAR in the O-IFU group were considered acceptable because there was no difference in overall survival rates and reintervention rates between the W-IFU and the O-IFU groups. Irrespective of IFU, morphological changes including neck angulation, neck diameter, sac re-expansion, and Palmaz stent displacement, were found. Therefore, careful long-term follow-up is required for all patients who undergo EVAR.

Acknowledgement

Disclosure Statement

All authors declare no conflict of interest.

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